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32

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,750	07/25/2005	Gregory B Martin	3213/104	6908
7590 Michael L Goldman Nixon Peabody Clinton Square P O Box 31051 Rochester, NY 14603-1051		06/28/2007	EXAMINER MAASHO, KERIMA K	
			ART UNIT 1609	PAPER NUMBER
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, 'if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/524,750	<b>Applicant(s)</b> MARTIN ET AL.	
	<b>Examiner</b> Kerima Maasho	<b>Art Unit</b> 1609	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 April 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-6 and 103-109 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 103-109 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 February 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

***Detailed action***

Applicant's election with traverse of claims 1-6 and 103-109 and SEQ ID No 2 in the reply filed on 04/23/2007 is acknowledged. The traversal is on the ground(s) that the invention groups are closely related and do not require separate search. This is not found persuasive because each product requires search not required by the others. The requirement is still deemed proper and is therefore maintained.

Claims 7-102 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 04/23/2007.

Claims 1-109 are pending in this application, however, the elected group of claims 1-6 and 103-109 are under consideration in this examination.

***35 U.S.C. 101 reads as follows:***

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

1. Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Applicants claim a bacterial effector protein which inhibits programmed cell death in eukaryotes. The protein is not recited as isolated or in some other fashion extracted from the bacteria, as claimed the bacteria and any protein it possesses are a product of nature. The recitation of the limitation

Art Unit: 1609

"isolated bacterial effector protein" or if the reference is the whole organism "cultured bacteria" would be remedial.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-6 and 103-109 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the inhibition of programmed cell death in eukaryotes, does not reasonably provide enablement for treating a subject with conditions mediated by a programmed cell death (PCD). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Art Unit: 1609

"The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." In the instant case applicants failed to disclose illustrative examples of mammalian situation (e.g. effect on mammalian cell culture or animal models) in which the invention may be utilized in the present specification. As the basis for the instant invention is to provide methods of treating a subject with conditions mediated by program cell death by administering the bacterial effector protein, it is therefore, important to give working examples that enables the procedure with specific dosage of the protein as well as the mode of administration. Given that the applicant failed to give working examples of any kind, a skilled person in the art would have to do undue experimentation to practice the claimed invention.

Scope of the invention: Applicants claim a method for treating conditions mediated by PCD in a subject, said method comprising: administering to a subject a bacterial effector protein which inhibits PCD under CONDITIONS EFFECTIVE TO TREAT THE CONDITION mediated by PCD. The scope of the claim is so broad as to encompass ANY conditions effective to treat PCD-mediated conditions.

Nature of the invention: The invention involves treating PCD mediated conditions such as Parkinson's disease, Alzheimer's disease, hepatitis, acute liver injury and inflammation with untested (lack of working examples in animal models) bacterial proteins. The disclosure provides working examples in plants only.

The state of the prior art: There has not been convincing evidence for the availability of universal PCD regulators/effectors. Lacomme et al (PNAS 1999, vol 96, pp 7956-61)

Art Unit: 1609

discusses that although PCD fulfills the same roles, elimination of unwanted cells during development and sacrifice of diseased cells, in both plants and animals evidence for common pathways leading to cell death is limited (p 5). It would appear that if the pathway for PCD induction is different in plants and animals the pathway to inhibit PCD would also be different.

Andersen (Bioessays 2001, vol 23, pp 640-6) discusses that the issues of anti-apoptotic therapies in relation to Parkinson's disease would be to deliver the required agents to the neurons in sufficient quantities for them to achieve their protective effects while not interfering with events in other cell types such as immune cells where prevention of apoptosis could result in chronic inflammation (p 644). Andersen further points out the importance of optimization of delivery of the various PCD inhibiting agents; for example too little apoptosis due to inappropriate over expression of bcl-might lead to oncogenesis. In the instant case, short of working example and guidance as to the mode of treatment in subjects with PCD mediated conditions, it would appear that the applicants are not in possession of a method of treatment.

Therefore, considering the state of the art, the limited guidance in the specification; the scope of the claims and the absence of working examples, undue experimentation would be required to practice the full scope of the invention.

***Claim Rejections - 35 USC § 102***

Art Unit: 1609

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Mangan et al (Infection and Immunity 1992 vol 60, pp 1684-6).

Claim 1 refers to a bacterial effector protein which inhibits PCD in eukaryotes. Mangan et al teach a bacterial endotoxin-associated protein that inhibits program cell death by inducing enhanced monocyte survival, cytokine release and receptor expression. Mangan et al further teach that LPS-stimulated monocytes produce IL-1, a cytokine that prevents monocyte PCD and upregulates numerous components of the host immune response. Claim 1 as claimed refers to any bacterial protein with the capacity of inhibiting PCD in eukaryotes. Therefore, Mangan et al's teaching anticipate the claimed invention.

4. Claims 1-6 are rejected under 35 U.S.C. 102(a) as being anticipated by either Kim YJ (Cell 2002, vol 109, pp 589-598) or Fouts DE (PNAS 2002, Vol 99, pp 2275-2280).

Art Unit: 1609

Claim 1 refers to a bacterial effector protein which inhibits PCD in eukaryotes. Claim 2 refers to the protein with SEQ ID No 2, with a motif selected from a group of sequences (claim 3), with an amino acid sequence of SEQ ID No 24 (claim 4), with an amino acid sequence spanning a C-terminus (claim 5) and a sequence spanning amino acid 308 and 553 of SEQ ID No 2 (claim 6).

Kim et al teach distinct *Pseudomonas* effector proteins that interact with pto kinase (p 589). One such protein is the AvrPtoB protein whose amino acid sequence reads on SEQ ID No 2 of the present application, as well as the motifs of claim 3, which are sub-regions in SEQ ID No 2, and SEQ ID No 24 the consensus of SEQ ID No 2-8. (See fig 1). Therefore, Kim et al fully anticipate claims 1-6.

Fouts et al also teach the identification of a bacterial effector protein AvrPtoB which reads on SEQ ID No 2 of the present invention (see tables 1 and 2). The sequence of the bacterial effector protein of Fouts et al's teaching could be found in UniProt. Fouts et al anticipates the limitations of the claims 1-6 of the present invention.

Therefore, the bacterial effector protein of the present invention is anticipated by both Kim et al and Fouts et al teachings.

### ***Conclusion***

Claims 1-6 and 103-109 are rejected for reasons as explained above.



Art Unit: 1609

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kerima Maasho whose telephone number is 571-270-3055. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mary Mosher can be reached on 571-272-0906. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



MARY MOSHER  
SUPERVISORY PATENT EXAMINER

6-25-07